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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/755,082	01/09/2004	Brian Dalby	IVGN 349	8189
52059 7590 07/05/2007 INVITROGEN CORPORATION C/O INTELLEVATE P.O. BOX 52050 MINNEAPOLIS, MN 55402			EXAMINER SCHNIZER, RICHARD A	
			ART UNIT	PAPER NUMBER
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			07/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/755,082	Applicant(s) DALBY ET AL.	
	Examiner Richard Schnizer, Ph. D.	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 11 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 118-135 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 118-135 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 09 January 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>6/11/07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

An amendment was received and entered on 6/11/07.

Claims 1-117 were cancelled and claims 118-135 were added as requested.

Claims 118-135 are pending and under consideration.

Specification

Applicant's submission of a substitute specification overcame the previous objections to the specification. The specification is objected to because the pages are not properly numbered. The specification begins with pages 1-46, after which occur pages numbered 44-48, and then 53-157. Appropriate renumbering is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 118-129, 134 and 135 are rejected under 35 U.S.C. 102(a) and 102 (e) as being anticipated by Berg et al (US 20020155099).

Berg taught methods of photochemical internalization of nucleic acids. Nucleic acids are complexed with vectors, such as antibodies or polylysine, that direct cellular uptake, and contacted to cells resulting in uptake into the endosome-lysosome pathway. Cells are also contacted with a fluorescent photosensitizer, which may be attached to

Art Unit: 1635

the delivery vector, and are finally subjected to illumination resulting in release of the nucleic acids from endosomes/lysosomes. See entire document, especially abstract and paragraphs 8-10, 43, 49.

Berg exemplified excitation of the fluorophore AIPCS_{2a} with light of a wavelength of 351-356 nm. See paragraphs 87 and 117.

Berg taught a variety of nucleic acid molecules that could be delivered by the method, including DNA, RNA, oligonucleotides, a 37 nucleotide 2'-O-methylated ribozyme, and double stranded plasmids encoding green fluorescent protein. See paragraphs 49, 85, and 114. Regarding claim 124, 37 nucleotides is considered to be "about" 30.

The polylysine of Berg is considered to be the cellular delivery molecule of the claims. The reference is considered to anticipate claims 128 and 129 because any portion of polylysine can be considered to be fused to any other part of polylysine (i.e. the first five residues of polylysine can be considered to form a fusion protein with the remaining polylysine residues). Either of these portions can be considered to be an "accessory" as required by claim 129.

Response to Arguments

Applicant's arguments filed 6/11/07 have been fully considered but they are not persuasive.

Applicant addresses the rejection at pages 7 and 8 of the response. Applicant argues that Berg does use fluorescein as a photosensitizer, and that the

Art Unit: 1635

photosensitizers of Berg are not the photosensitizers of the instant invention. This is unpersuasive because the instant claims do not limit the nature of the fluorescent molecule. Applicant asserts that the instant specification at page 110-112 describes fluorescent molecules that are different from those described in Berg. This is unpersuasive because although the instant specification discloses different fluorescent molecules than Berg, it explicitly states that fluorescent moieties and molecules useful for practicing the invention are not limited to those disclosed in the specification. See paragraph 283. Accordingly, the scope of the fluorescent molecules embraced by the claims is not limited to those disclosed in the specification, and clearly embraces those taught by Berg. Applicant argues that the photosensitizers of Berg are not fluorescent molecules as the term is used in the instant claims because the photosensitizers of Berg disrupt endosomal membranes, but the instantly claimed fluorescent molecules do not. This is unpersuasive because Applicant is arguing limitations that are not in the claims (lack of membrane disruption), and because Applicant has presented no evidence to support the opinion that the fluorescent molecules disclosed in the specification would not damage endosomal membranes. For these reasons the rejection is considered proper and is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

Art Unit: 1635

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 118 and 128-133 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wahl (US 5654182) in view of Berg et al (US 20020155099).

Wahl taught a method for the integration of a first nucleic acid into the genome of a mammalian host cell, said method comprising stably integrating a first FLP recombination target site (FRT) into-said genome; and introducing into said mammalian host cell of step a) an FLP recombinase and said first nucleic acid, wherein said first nucleic acid comprises a second FRT, and wherein said FLP recombinase catalyzes recombination between said first FRT and said second FRT, thereby precisely targeting integration of said first nucleic acid into said genome at the site of said first FRT. The recombinase will, absent evidence to the contrary, form a complex with the nucleic acid due to the fact that it is a nucleic acid binding protein. The recombinase can be considered to be a fusion of different domains, e.g. nucleic acid binding domains and a catalytic domain.

Wahl did not teach contacting the cell with a fluorescent molecule, a cellular delivery molecule, or treating the cell with a treatment that results in dissociation from the nucleic acid of either the fluorescent molecule or the cellular delivery molecule.

Berg taught methods of photochemical internalization of nucleic acids. Nucleic acids are complexed with vectors, such as antibodies or polylysine, that direct cellular uptake, and contacted to cells resulting in uptake into the endosome-lysosome pathway. Cells are also contacted with a fluorescent photosensitizer, which may be attached to the delivery vector, and are finally subjected to illumination resulting in release of the

Art Unit: 1635

nucleic acids from endosomes/lysosomes. See entire document, especially abstract and paragraphs 8-10, 43, 49.

It would have been obvious to one of ordinary skill in the art at the time of the invention to deliver the nucleic acid of Wahl using the method of Berg. One would have been motivated to do so because the method of Berg facilitates release from endosomes, thereby limiting the amount of transfecting nucleic acid lost to lysosomal degradation. Note that Wahl envisions adding the recombinase simultaneously with the nucleic acid to be delivered. Note also that the recombinase of Wahl can be considered to be a cellular delivery polypeptide inasmuch as it catalyzes the delivery of a nucleic acid into the genome of a cell. The recombinase can also be considered to be a fusion protein, i.e. the N-terminal half of the recombinase is fused to the C-terminal half.

Thus the invention as a whole was prima facie obvious.

Response to Arguments

Applicant's arguments filed 6/11/07 have been fully considered but they are not persuasive.

Applicant addresses the rejection at pages 8 and 9 of the response.

Applicant argues that the recombinase of Wahl cannot be considered to be a cellular delivery polypeptide because the instant specification at paragraph 23 on page 4 defines such molecules as those that facilitate translocation into a cell, not into a genome. This is unpersuasive because the passage relied upon by Applicant refers to

Art Unit: 1635

that "a cellular delivery molecule that can facilitate the translocation of the complex or portion thereof into cells." This passage in now way limits the definition of a cellular delivery molecule such that the Office's broad but reasonable interpretation would be excluded. Applicant also reiterates arguments against the photosensitizers of the Berg reference. These arguments are unpersuasive for the reasons given above under 35 USC 102 rejections.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Art Unit: 1635

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

A handwritten signature in black ink, appearing to read 'R. Schnizer', with a long horizontal flourish extending to the right.

Richard Schnizer, Ph.D.
Primary Examiner
Art Unit 1635